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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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09/350,518

07/09/1999

JOHN C. REED

066654-0515

8259

41552 7590 06/17/2010
MCDERMOTT, WILL & EMERY
11682 EL CAMINO REAL
SUITE 400
SAN DIEGO, CA 92130-2047

EXAMINER

SANG, HONG

ART UNIT

PAPER NUMBER

1643

NOTIFICATION DATE

DELIVERY MODE

06/17/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SIP_Docket@mwe.com

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 09/350,518 | Applicant(s) REED, JOHN C. | |
| | Examiner HONG SANG | Art Unit 1643 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81 and 83-109 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

RE: Reed

1. Applicant's response filed on 5/11/2010 is acknowledged. Claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 are pending. Claims 1-10, 13-15, 17-21, 28-31, 35-43, 45-49, 55, 57, 70-72 and 82 have been cancelled. Claims 11, 16, 22-27, 32, 34, 44, 50-53, 56, 58-68, 74-79, 81, 83, 84, and 86-99 have been amended
2. Claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 are under examination.

Rejections Maintained

Claim Rejections - 35 USC § 102

3. The rejection of claims 11, 16, 24-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 75-79, 81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 102(b) as being anticipated by Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

The response states that the Office is improperly using the disclosure of Krajewski et al. and Exhibit 2 to support the anticipation rejection over the disclosure of Turner et al. It appears that the Office is using the disclosure of Krajewski et al. and Exhibit 2 to explain the meaning of the term "invasive carcinoma," also referred to as "IC," as disclosed by Turner et al. The response states that extrinsic evidence may be used to explain but not expand the meaning of terms and phrases used in the reference

Art Unit: 1643

relied upon as anticipatory of the claimed subject matter. The Office is using the disclosure of Krajewski et al. in combination with Exhibit 2 to fill in gaps and expand the disclosure of Turner et al. The response states that invasive carcinoma, as taught by Turner, could include stage I, II, III, or IV breast cancers or any of the thirteen TNM stage groupings. Absent the disclosure of Krajewski et al., Turner et al. are silent as to whether the breast cancer samples were stage I, II, III or IV or any of the thirteen TNM stage groupings. Furthermore, the method described by Turner et al. is a retrospective study, whereas the claimed methods are prognostic. Turner et al. describe a retrospective study that showed no statistically significant correlation between invasive carcinoma patient's survival and overexpression of cytoplasmic BAG-1. The disclosure of Turner et al. as evidenced by Krajewski et al., actually teaches away from the claimed methods. At best, Krajewski et al. disclose higher levels of BAG-1 nuclear immunostaining (>20%) correlated with longer OS among patients with early stage breast cancer (p0.001) (see page 36, first column, lines 19-23).

Applicants' arguments and submitted evidence have been carefully considered but are not persuasive.

A rejection under 35 U.S.C. 102 over multiple references has been held to be proper when the extra references are cited to: (A) prove the primary reference contains an "enabled disclosure," (B) explain the meaning of a term used in the primary reference; or (C) show that a characteristic not disclosed in the reference is inherent (see MPEP 2131.01).

It is proper to use extrinsic evidence to explain the meaning of terms and phrases used in the reference relied upon as anticipatory of the claimed subject matter.

Art Unit: 1643

Krajewski is cited as evidence to show that the invasive carcinoma disclosed in Turner's reference is early stage invasive cancer. Early stage invasive breast cancer includes stages I and II breast cancer, as evidenced by Exhibit 2 submitted by applicants on 7/23/2008 (see page 3). Krajewski and Exhibit 2 are provided to explain the information present in Turner's reference and do not expand the meaning of the term used in Turner's reference. Evidence can be provided by the post filing date art because it is just explaining the information present in the prior art and does not change or otherwise modify what is taught in the prior art. The invasive breast cancer studied in the Turner's reference was stages I and II, irrespective of the examiner's reliance on Krajewski and Exhibit 2. Applicant's arguments of retrospective study and lacking statistic significance are not persuasive because the standard for a 102(b) reference is that the reference must teach every limitation of the claim. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Because Turner teaches each and every element set forth in the claims, Turner anticipates the instant invention. Finally applicant's arguments of teaching away are not persuasive because the instant rejection is a 102(b) rejection and the standard of teaching away does not apply. Krajewski and Exhibit 2 are merely used to explain the information present in Turner's reference.

With respect to new claim limitation "cytosolic BAG-1", Turner disclosed that 10-year OS [overall survival] and DDFS [distant disease free survival] for patients with overexpression of cytoplasmic BAG- 1 in IC [invasive carcinoma] specimens was 75%

Art Unit: 1643

and 70%, respectively, as compared with 62% and 35% for tumors with low cytoplasmic BAG-1 levels (p=0.06).

Claim Rejections - 35 USC § 103

4. The rejection of claims 11, 12, 16, 24-27, 32-34, 44, 50-54, 56, 58-61, 67-69, 75-81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sano et al. (US patent NO. 5665539), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained

Applicant's presented same arguments as for 102(b) rejection and these arguments are not persuasive for the reasons set forth above.

5. The rejection of claims 11, 16, 24-27, 32, 34, 44, 50-54, 56, 58-68, 75-79, 81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Sauter et al. (British Journal of Cancer, 1997, 76(4): 494-501), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

Applicant's presented same arguments as for 102(b) rejection and these arguments are not persuasive for the reasons set forth above.

Art Unit: 1643

6. The rejection of claims 11, 16, 24-27, 32, 34, 44, 50-54, 56, 58-68, 75-79, 81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print) in view of Love (US Patent No. 6,221,622B1, Date of Patent 4/24/2001, earliest effective filing date 4/28/1998), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

Applicant's presented same arguments as for 102(b) rejection and these arguments are not persuasive for the reasons set forth above.

7. The rejection of claims 11, 16, 22-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 73-79, 81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), in view of Mather et al. (Clin. Cancer Res., 1998, Aug., 4:1851-1856), and McGuire et al. (US 5,188,964, Date of Patent: 2/23/1993), as evidenced by Krajewski et al. (Endocrine-Related Cancer, 1999, March, 6(1):29-40) and Exhibit 2 submitted by applicants on 7/23/2008 is maintained.

Applicant's presented same arguments as for 102(b) rejection and these arguments are not persuasive for the reasons set forth above.

8. The rejection of claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81, and 83-109 under 35 U.S.C. 103(a) as being unpatentable over Turner et al. (Breast Cancer Research and Treatment (Oct. 1997), 46(1): p69, print), in view of Mather et al. (Clin.

Art Unit: 1643

Cancer Res., 1998, Aug., 4:1851-1856), McGuire et al. (US 5,188,964, Date of Patent: 2/23/1993), Sano et al. (US patent NO. 5665539), and Love (US Patent No. 6,221,622B1, Date of Patent 4/24/2001, earliest effective filing date 4/28/1998).

The response states that Turner et al. describe a retrospective study that showed no statistically significant correlation between invasive carcinoma patient's survival and overexpression of cytoplasmic BAG-1. Turner does not teach early stage invasive cancer.

Applicant's arguments have been carefully considered but are not persuasive. Although Turner's reference discloses retrospective study, the method steps taught by Turner are the same as the instant claims. Applicant's arguments of p value are not persuasive because p value is not a factor for determining the obviousness. Moreover it is known in the art that p value is dependent from many factors such as patient population (size of the patient population, percentage of stage I and stage II in the patient population), sample preparation, detection methods, etc. With respect to early stage invasive cancer, both Maher and McGuire et al. teach that there is a great need for a general method of predicting tumor recurrence in early stage breast cancer patients. Given the teachings of Turner that subcellular location of BAG-1 may have prognostic importance with respect to survival of breast cancer patients, one skilled in the art would have been motivated to use the method of Turner for predicting the disease-free or overall survival of early stage (stages I and/or II) breast cancer patients. One would have had a reasonable expectation of success because Turner et al. have shown that the 10-year overall survival (OS) and distant disease free survival (DDFS)

Art Unit: 1643

for breast cancer patients with overexpression of BAG-I in IC specimens was 75% and 70%, respectively, compared to 62% and 35% for tumors with low cytoplasmic BAG-I levels.

For the forgoing reasons, the rejection is maintained.

Conclusion

9. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

Art Unit: 1643

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/
Examiner, Art Unit 1643
/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643